REMARKS

I. Status of the Claims

Claims 275, 289, 290 and 296-301 were pending and examined in the March 7, 2011 Office Action. Claims 289, 290 and 298-301 were withdrawn and claims 275, 296 and 297 were examined therein. With this reply, claim 275 is amended. The claim amendment is made without prejudice or disclaimer and provides no new matter. Claims 275, 296 and 297 are presented for reconsideration.

II. Rejections under 35 U.S.C. § 102

Claims 275 and 296 are rejected under 32 U.S.C. 102(e) as anticipated by Cantor et al. (US 5,561,043). Applicants request reconsideration and withdrawal of this rejection in light of the following discussion.

The instant claims are directed to

> An isolated multimeric composition comprising a binding matrix and more than one monomeric unit, wherein each monomeric unit comprises two elements covalently attached to one another, wherein a first element is a protein, wherein said protein is a ligand to a cell surface receptor, wherein a second element is a single-stranded polynucleotide and wherein each monomeric unit is separately attached to said binding matrix through said second element via hydrogen bonding between said single-stranded polynucleotide of said monomeric unit and said binding matrix, wherein said binding matrix is a polynucleotide comprising a sequence complementary to said single-stranded polynucleotide.

Claim 275. Cantor et al. describe a multimeric nucleic acid construct to which is bound one, two, three or more nucleic acids species. As described therein, "[t]he nucleic acids may comprise **a** double-stranded portion..." (emphasis added), to which a functional group (*e.g.*, a hormone) may be attached, for example as illustrated in FIG. 1B of Cantor et al. This differs from the composition of claim 275 in that Cantor et al. teaches only one double-stranded portion attached to the nucleic acid species, whereas the composition claimed herein has multiple double stranded portions, each with an attached ligand. Although the system described in Cantor et al. is designed to provide multiple functional groups, the multiple functional groups are achieved by hybridization

of a nucleic acid-functional group unit to the multiple nucleic acid species present in the branching arrangement created by having multiple nucleic acid species attached to a streptavidin and/or by hybridization of the nucleic acid species from two streptavidin molecules, where only one nucleic acid-functional group unit is attached to an individual nucleic acid species. By contrast, the instant invention provides multiple nucleic acid-protein units on a single nucleic acid, as illustrated in FIG. 22 of the instant specification. Thus, Cantor et al. do not teach or suggest a binding matrix that is a polynucleotide to which more than one monomeric unit is separately attached, as claimed in the instant claims.

Based on the above discussion, it is clear that Cantor et al. do not teach or suggest every element of the instant claims, and thus do not anticipate the claims. Applicants therefore respectfully request withdrawal of the rejection under 35 U.S.C. 102(e).

III. Rejections under 35 U.S.C. § 103

(a) Claims 275 and 296-297 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al. (described under **II.** above) in view of Osborne et al. (PNAS, 1976,73:4536-4540). The Office Action asserts that Cantor et al. teach all elements of the claims except that hormones include insulin, which is taught by Osborne et al. Applicants respectfully request reconsideration and withdrawal of this rejection in light of the following comments.

As discussed under **II.** above, Cantor et al. do not teach or suggest multiple nucleic acid-protein units on a single nucleic acid, since all relevant constructs taught or suggested by Cantor et al. have only a single nucleic acid-protein unit on any particular nucleic acid. Osborne et al. also do not teach or suggest multiple nucleic acid-protein units on a single nucleic acid. As such, the combination of references do not teach or suggest all of the claim elements and therefore do not make the instant claims obvious. Withdrawal of this rejection is therefore respectfully requested.

(b) Claims 275 and 296-297 are rejected under 35 U.S.C. 103(a) as being unpatentable over Priest (US 5,391,723) in view of Osborne et al. (described under **(a)** above). The Office Action asserts that Priest teaches all elements of the claims except (i) a multimer of the monomeric units recited in the instant claims, and (ii) that insulin can be a targeting molecule. The Office Action further asserts that Osborne et al. teach the latter and the former is an obvious variation since "one or ordinary skill in the art would have been motivated to make a combination product comprising multiple identical monomeric units of insulin, wherein each monomeric unit of insulin is covalently bound to a single-stranded oligonucleotide linker, which in turn is hybridized to a single-stranded oligonucleotide." Office Action at p. 6. To rationalize that the skilled artisan would "obviously" imagine that multiple monomeric units of Priest could be hybridized to a single oligonucleotide, the Office Action cites *In re Kerkhoven* that "It is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose...." However, Applicants note that the Office Action does not establish that hybridizing multiple monomeric units to a single polynucleotide is taught in the prior art, since no reference cited in the Office Action teaches or suggests such a configuration. Instead, the PTO simply identified the protein-nucleic acid monomer of Priest, then, not being able to find any reference that teaches multiple protein-nucleic acid multimers on a single polynucleotide as claimed, rationalizes that such a configuration is obvious by using impermissible hindsight knowledge of the instant invention. Thus, the law as taught in *In re Kerkhoven* is irrelevant because multiple protein-nucleic acid multimers on a single oligonucleotide is **not** taught in the prior art.

MPEP 2142 states,

> To reach a proper determination under 35 U.S.C. 103, the examiner must step backward in time and into the shoes worn by the hypothetical "person of ordinary skill in the art" when the invention was unknown and just before it was made. In view of all factual information, the examiner must then make a determination whether the claimed invention "as a whole" would have been obvious at that time to that person. Knowledge of applicant's disclosure must be put aside in reaching this determination, yet kept in mind in order to determine the "differences,"

> conduct the search and evaluate the "subject matter as a whole" of the invention. The tendency to resort to "hindsight" based upon applicant's disclosure is often difficult to avoid due to the very nature of the examination process. However, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art.

Here, it is clear that putting more than one of the protein-nucleic acid monomers of Priest onto a single polynucleotide would not be obvious to the skilled artisan since such a configuration is not taught or suggested in any cited reference. Thus, the PTO could only have gleaned the suggestion of multiple protein-nucleic acid monomers on a single polynucleotide from the instant specification, using impermissible hindsight.

In light of the above discussion it is clear that the combination of references do not make the instant claims. Withdrawal of this obviousness rejection is therefore respectfully requested.

IV. Double Patenting Rejections

Claims 275 and 296-297 are provisionally rejected on the ground of obviousness-type double patenting (ODP) as being unpatentable over claims 246 and 264-265 of copending Application No. 08/978,632. Since this rejection is dependent on the scope of the final claims in both the instant application and application 08/978,632, Applicants will provide a terminal disclaimer where necessary when a proper ODP rejection is the only rejection remaining in this application.

V. Conclusion

In view of the foregoing remarks, Applicants respectfully request withdrawal of the rejections of record and examination of withdrawn claims 289, 290, and 298-301, as provided under MPEP 821.04, since the withdrawn claims have all the limitations of allowable claim 275.

The United States Patent and Trademark Office is hereby authorized to charge the extension of time and Request for Continued Examination fees, as well as any other fees required to maintain pendency of this application, to Deposit Account No. 05-1135.

If a telephone conversation would further the prosecution of the present application, Applicants' undersigned attorney requests that he be contacted at the number provided below.

Respectfully submitted,

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